Skin rash in a patient with A(H1N1) infection

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Dear Editor,

In December 2009, a 43-year-old, mechanically ventilated patient with acute respiratory distress syndrome (ARDS) due to A(H1N1) influenza infection was transferred to our intensive care unit (ICU) for extracorporal membrane oxygenation. Prior to admission to the first hospital, the patient had been in good health; his personal history was unremarkable, except for obesity (body mass index 41 kg/m^2) and a borderline personality disorder with intermittent alcohol abuse. The A(H1N1) infection resolved following treatment with oseltamivirr; however, his clinical condition subsequently worsened again, characterized by severe hemodynamic impairment with excessive need for vasoactive compounds, including norepinephrine (up to 90 g/min) and vasopressin (up to 0.04 U/min). Bacterial sepsis was excluded based on repetitive negative blood cultures. Sharply demarcated erythematous skin lesions developed simultaneously on the trunk, arms, and legs (Fig. 1a). Differential diagnosis included allergic reaction to several medications, eosinophilic cellulitis (Muckle–Wells' syndrome), and small-vessel vasculitis or infectious vasculitis.

Laboratory evaluation showed peripheral eosinophilia, thrombocytopenia, and progredient liver failure; alanine aminotransferase was 105 U/l, the international normalized ratio was 2.0, and the production of both albumin and coagulation factors was reduced (albumin 14 g/l; factor V 39%, II 39%, VII 23%). Viral RNA for novel influenza A(H1N1) was no longer detectable in nasal and pharyngeal swabs. Serologic testing for hepatitis B and C and autoimmune antibodies, including anti-smooth muscle (anti-Sm) and antimitochondrial (AMA) antibodies, were negative. PCR assay results for herpes simplex type 1 and 2, varicella zoster, Epstein–Barr virus, and human herpes virus 6 were also negative. However, the PCR assay was positive for CMV, detecting viral loads up to a level of 5 million copies per milliliter. Skin biopsies were performed and showed discrete lymphocytic inflammation and characteristic nuclear inclusion bodies [1] within the vascular endothelial cells ("owl's eyes"; Fig. 1b). CMV infection of the vessels was confirmed by PCR. Antiviral treatment with ganciclovir was initiated, and the rash disappeared promptly, allowing the amount of vasoactive pressors to be reduced. Forty-seven days after the initiation of antiviral therapy, viral loads were no longer detectable by PCR.

Infections with CMV, a member of the herpesvirus family with high seroprevalence in the adult population, are of major concern in neonates and in patients with significant immunosuppression, in particular in those with acquired immune deficiency syndrome (AIDS) and transplant recipients. Both de novo infection and reactivation of the latent state of the virus usually lead to severe illness in these patients, whereas clinically apparent disease does not occur in the vast majority of infections in immunocompetent hosts. Common organ-specific complications of CMV infection include liver function abnormalities, gastrointestinal manifestations, Guillan–Barré syndrome, pneumonitis, and retinitis. Moreover, reactivation of CMV infection is commonly observed in critically ill patients and is associated with disease severity, prolonged hospitalization in the ICU, and mortality

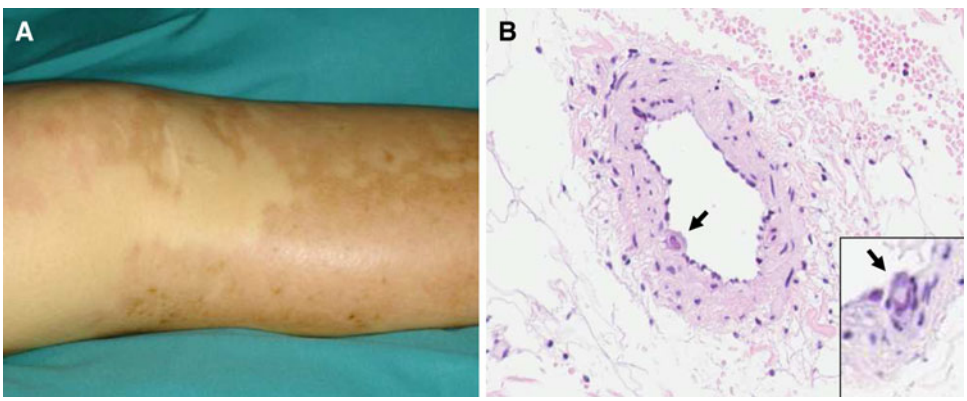

Fig. 1 **a** Erythematous, macular rash, sharply demarcated within hypopigmented areas. **b** Skin biopsy samples revealing discrete lymphocytic infiltration surrounding the perivascular tissue; cytomegalovirus (CMV)-specific inclusion bodies within vascular endothelial cells (*arrow*) presenting as characteristic "owl's eyes" (*inset*)

[2, 3]. Cutaneous manifestations, however, appear to be rare clinical entities [4, 5]. Our case thus illustrates the importance of recognizing and treating CMV infection in non-immunosuppressed patients in the ICU, in particular in those with unexplained rash.

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